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Osha Liang LLP, Smith & Nephew, Inc.
150 Minuteman Road
Andover, MA 01810

EXAMINER	
PEPITONE, MICHAEL F	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Response to Amendment

Applicant's arguments filed 12/16/10 have been fully considered but they are not persuasive. While the amendment after final has been entered, the claims finally rejected in the action mailed 9/16/10 is maintained. The rejection of claims 1-10, 12-14, 17-19, 25-26, and 29-32 based upon Brocchini et al. (US 2002/0082362) and Neuenschwander et al. (US 5,665,831) is maintained for reason of record and following response.

Brocchini et al. (US '362) disclose biodegradable polyacetal polymer (abstract; ¶ 3, 16-20), wherein of polymer of Formula (I) (¶ 63-81) is prepared by reacting a diol of Formula (II) with divinyl ether of Formula (III) (¶ 82-86). Brocchini et al. (US '362) disclose Formula (I) containing polyamides (¶ 74-78). Brocchini et al. (US '362) disclose a conjugate bioactive compound (compound 16; ¶ 96-106, 165-167). Brocchini et al. (US '362) disclose the diol may also comprise any diol suitable for use in biomaterials (¶ 91).

Brocchini et al. teaches the diol of Formula (II) is a polyethylene glycol or polypropylene glycol having a molecular weight in the range of 100-20,000, most preferably 200-5,000, in particular a polyethylene glycol having a molecular weight of approximately 200-4,000 (¶ 91). Brocchini et al. (US '362) disclose Formula (I) containing polyamides (¶ 74-78). Brocchini et al. teaches a specific embodiment (ex. 1; polyacetal 3) comprising the reaction of poly(ethylene glycol) {mw = 3,400 g/mol} with tri(ethylene glycol) divinyl ether in the presence of p-toluenesulfonic acid (¶ 151-153) [see ex. 7 as well (¶ 169-178)].

While ex. 1, polyacetal 3 disclosed by Brocchini et al. employs PEG 3400 {mw = 3,400 g/mol; mp 54-58 °C}, Brocchini et al. disclose the diol of Formula (II) is polyethylene glycol {PEG} having a molecular weight in the range of 100-20,000 (¶ 91); i.e. Brocchini et al. disclose

PEGs having molecular weights in the range of 100-20,000, with specific PEGs {PEG 7,500; PEG 20,000} having melting points {mp} of ~60-64 °C. Additionally, a compound which is water soluble at 37 °C does not preclude it from having a melting point above 37 °C {see remarks, pg. 15}. For example, sodium chloride NaCl is soluble in water at 37 °C {357 mg/ml at 25 °C} and has a melting point of 804 °C. It is unclear to the examiner how Applicant correlates the melting point of a compound and its solubility.

[Note: Poly(ethylene glycol) 3,400 (**CAS Number:** 25322-68-3) {mw = 3,400 g/mol} has a melting point of 54-58 °C. {http://www.polysciences.com/Catalog/Department/Product/98/categoryId__289/productId__59/}; Poly(ethylene glycol) 7,500 (**CAS Number:** 25322-68-3) {mw = 7,500 g/mol} has a melting point of 60-63 °C. {http://www.polysciences.com/Catalog/Department/Product/98/categoryId__289/productId__421/}; Poly(ethylene glycol) 20,000 (**CAS Number:** 25322-68-3) {mw = 20,000 g/mol} has a melting point of 61-64 °C. {http://www.polysciences.com/Catalog/Department/Product/98/categoryId__289/productId__1368/}].

Neuenschwander et al. (US '831) disclose biocompatible block copolymers (abstract) comprising macrodiols based on α,ω-dihydroxypolyethers and α,ω-dihydroxypolyesters (2:9-20), wherein the macrodiols based on α,ω-dihydroxypolyesters are obtained by ring opening polymerization of lactones {dilactide, diglycolide, ε-caprolactone}(2:26-41; see examples). Neuenschwander et al. (US '831) teaches the copolymer can contain a conjugate antibiotic (9:25-31). Neuenschwander et al. (US '831) disclose the polymers are biodegradable (11:20-22).

As Brocchini et al. (US '362) disclose the diol may also comprise any diol suitable for use in biomaterials, and Neuenschwander et al. (US '831) disclose biocompatible block copolymers comprising macrodiols based on α,ω-dihydroxypolyethers and α,ω-dihydroxypolyesters, one having ordinary skill in the art would have been motivated to employ α,ω-dihydroxypolyesters as the diol in the composition of Brocchini et al. (US '362) because Brocchini et al. (US '362) suggest any diol suitable for use in biomaterials and Neuenschwander et al. (US '831) disclose biocompatible block copolymers comprising macrodiols based on α,ω-dihydroxypolyesters [see MPEP 2144.06].

Applicant's arguments that the block copolymers having a melting point between 80 °C and 200 °C disclosed by Neuenschwander et al. (US '831) would not be employed as the diol in the composition of Brocchini et al. (US '362), because Brocchini et al. (US '362) requires the composition to be soluble at 37 °C are not persuasive. The examiner notes Brocchini et al. (US '362) employs PEG 3400 having a melting point of 54-58 °C {see above}; i.e. Brocchini et al. (US '362) utilizes compounds which are solid above 37 °C, yet are soluble at 37 °C. Therefore, compounds which melt above 37 °C {ex. PEG 3400, mp 54-58 °C} afford operative subject matter in Brocchini et al. (US '362). Neuenschwander et al. (US '831) was relied on for the macrodiols {α,ω-dihydroxypolyesters} (2:9-54; see examples 1-8; 11:20-14:36), not the entire block copolymer {mp 80 °C - 200 °C} prepared by linking the macrodiol with diisocyante {resulting in a polyurethane}, diacid halide, {resulting in a polyester}, or phosgene {resulting in a polycarbonate} (2:9-20). Neuenschwander et al. (US '831) disclose macrodiols {α,ω-dihydroxypolyesters} prepared from caprolactone, lactide, and aliphatic polyesters {via (R)-3-

hydroxybutyric acid} having molecular weights of about 300 to 10,000 Daltons (2:21-54; 3:1-7:46; examples 1-8; 11:20-14:36).

The rejection of claim 11 based upon Brocchini et al. (US 2002/0082362), Neuenschwander et al. (US 5,665,831), and Shalaby (US 6,503,991) is maintained for reason of record and following response.

Applicants' arguments regarding Brocchini et al. (US '362) and Neuenschwander et al. (US '831) have been sufficiently addressed above. Shalaby (US '991) was relied on for disclosing biocompatible block copolymers (abstract) comprising a pre-polymer prepared from an alkanediol containing a carbonate linkage (1:61-2:3), which provide biomedical articles having controlled absorption and reduced hydrolytic instability (2:34-42).

The rejection of claims 15, 25, and 27 based upon Brocchini et al. (US 2002/0082362), Neuenschwander et al. (US 5,665,831), and Wise et al. (US 6,071,982) is maintained for reason of record and following response.

Applicants' arguments regarding Brocchini et al. (US '362) and Neuenschwander et al. (US '831) have been sufficiently addressed above. Wise et al. (US '982) was relied for disclosing bioerodible polymers (abstract) comprising buffers such as calcium phosphate (5:21-59) and calcium phosphate fibers (6:58-59), as calcium carbonate and calcium phosphate counteracts the effects of irritation, inflammation, and swelling caused by acidic products generated upon hydrolysis within the body (5:21-39).

The rejection of claims 20 and 22 based upon Brocchini et al. (US 2002/0082362), Neuenschwander et al. (US 5,665,831), and Pathak et al. (US 6,923,986) is maintained for reason of record and following response.

Applicants' arguments regarding Brocchini et al. (US '362) and Neuenschwander et al. (US '831) have been sufficiently addressed above. Pathak et al. (US '986) was relied on for disclosing biodegradable polymers for use in drug delivery and biomedical applications (1:16-18), wherein additives such as antibiotics, antivirals, drugs and growth factors can be used in the composition; with specific growth factors including fibroblast growth factor {FGF} (11:8-36) and bone morphogenetic protein {BMP} (11:37-59).

The rejection of claim 21 based upon Brocchini et al. (US 2002/0082362), Neuenschwander et al. (US 5,665,831), and Törmäla et al. (US 6,579,533) is maintained for reason of record and following response.

Applicants' arguments regarding Brocchini et al. (US '362) and Neuenschwander et al. (US '831) have been sufficiently addressed above. Törmäla et al. (US '533) was relied on for disclosing bioabsorbable polymers containing antibiotics for use biomedical applications (1:5-26), wherein specific antibiotics include vancomycin (7:27-37).

The rejection of claim 23 based upon Brocchini et al. (US 2002/0082362), Neuenschwander et al. (US 5,665,831), and Uhrich (US 2002/0071822) is maintained for reason of record and following response.

Applicants' arguments regarding Brocchini et al. (US '362) and Neuenschwander et al. (US '831) have been sufficiently addressed above. Uhrich (US '822) was relied on for biocompatible/degradable polymers containing bioactive compounds (¶ 7), wherein specific bioactive compounds include doxorubicin and methotrexate (¶ 42).

The rejection of claim 24 based upon Brocchini et al. (US 2002/0082362), Neuenschwander et al. (US 5,665,831), and Heller et al. (US 7,045,589) is maintained for reason of record and following response.

Applicants' arguments regarding Brocchini et al. (US '362) and Neuenschwander et al. (US '831) have been sufficiently addressed above. Heller et al. (US '589) was relied on for biodegradable polymers (1:9-12; 5:3-16) containing active agents such as anti-inflammatory agents including ketorolac; and local anesthetics such as lidocaine and bupivacaine (8:22-67).

For convenience, the relevant text of the claims finally rejected on 9/16/10 is listed below.

Claims 1-10, 12-14, 16-19, 25-26, and 29-32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Brocchini et al. (US 2002/0082362) as applied to claim 1 above, in further view of Neuenschwander et al. (US 5,665,831).

Regarding claims 1-2, 7-10, 12-13, and 16: Brocchini et al. teaches a biodegradable polyacetal polymer (abstract; ¶ 3, 16-20), wherein of polymer of Formula (I) (¶ 63-81); is prepared by reacting a diol of Formula (II) with a divinyl ether of Formula (III) (¶ 82-86); wherein the diol of Formula (II) is a polyethylene glycol or polypropylene glycol having a molecular weight in the range of 100-20,000, most preferably 200-5,000, in particular a polyethylene glycol having a molecular weight of approximately 200-4,000 (¶ 91). Brocchini et al. (US '362) disclose Formula (I) containing polyamides (¶ 74-78). Brocchini et al. teaches a specific embodiment (ex. 1; polyacetal 3) comprising the reaction of poly(ethylene glycol) {mw = 3,400 g/mol} with tri(ethylene glycol) divinyl ether in the presence of p-toluenesulfonic acid (¶ 151-153) [see ex. 7 as well (¶ 169-178)]. Brocchini et al. teaches the diol may also comprise any diol suitable for use in biomaterials (¶ 91).

Brocchini et al. does not a specific diol comprising polyesters. However, Neuenschwander et al. teaches biocompatible block copolymers (abstract) comprising macrodiols based on α,ω-dihydroxypolyethers and α,ω-dihydroxypolyesters (2:9-20), wherein the macrodiols based on α,ω-dihydroxypolyesters are obtained by ring opening polymerization of lactones {dilactide, diglycolide, ε-caprolactone} (2:26-41; see examples). Neuenschwander et al. teaches the molecular weight of the macrodiol of about 300 to 10,000 daltons (2:43-54), and the resulting copolymer can contain a conjugate antibiotic (9:25-31). Brocchini et al. and Neuenschwander et al. are analogous art because they are concerned with a similar technical difficulty, namely the preparation of biocompatible block copolymers containing conjugate bioactive compounds prepared from (macro)diols. At the time of invention a person of ordinary skill in the art would have found it obvious to have combined α,ω-dihydroxypolyesters obtained by ring opening polymerization of lactones {dilactide, diglycolide, ε-caprolactone}, (2:26-41) having molecular weights of about 300 to 10,000 daltons, as taught by Neuenschwander et al. in the invention of Brocchini et al., and would have been motivated to do so since Neuenschwander et al. suggests that α,ω-dihydroxypolyethers and α,ω-dihydroxypolyesters are equivalent macrodiols (2:9-20) [see MPEP 2144.06].

Regarding claim 3: Brocchini et al. teaches a specific embodiment (ex. 5; ¶ 161-166) comprising the reaction of poly(ethylene glycol) {mw = 3,400 g/mol} with an amino functionalized bis-vinyl ether monomer {containing a diamide bond (diamino acid ester)} (compound 11; ¶ 161-164) in the presence of p-toluenesulfonic acid (¶ 165-166).

Regarding claim 4-5, 18, 29-32: Brocchini et al. teaches a specific embodiment (ex. 6; ¶ 167-168) comprising the reaction of poly(ethylene glycol) {mw = 3,400 g/mol} with an achiral bis-vinyl ether monomer having a conjugate bioactive compound (compound 16; ¶ 96-106, 167) in the presence of p-toluenesulfonic acid (¶ 165-166) {the as synthesized polymer-drug conjugate is a medical device}. Brocchini et al. teaches the polymer-drug conjugate as a pill/tablet, or contained in a carrier {coated medical device}.

Regarding claims 6, 14, 17, 19, and 25-26: Brocchini et al. teaches the polymer-drug conjugate of the invention (¶ 109, 112, 167-168) can be combined with preserving agents (¶ 110), pharmaceutically acceptable liquid carriers (¶ 112) and excipients such as polysacchrides and sodium chloride (¶ 115).

Brocchini et al. does not teach a specific embodiment comprising the polymer-drug conjugate of the invention (¶ 112, 167-168) combined with preserving agents, pharmaceutically acceptable liquid carriers, such as aqueous dextrose and glycols, or excipients such as polysaccharides {starch} and sodium chloride. However, at the time of invention a person of ordinary skill in the art would have found it obvious to have prepared the polymer-drug conjugate with preserving agents, pharmaceutically acceptable liquid carriers, such as aqueous dextrose and glycols, or excipients such as polysaccharides {starch} and sodium chloride based on the invention of Brocchini et al., and would have been motivated to do so since Brocchini et al. suggests that intravenous injectable composition can be prepared using preserving agents, pharmaceutically acceptable liquid carriers, such as aqueous dextrose and glycols (¶ 110, 112); and lyophilized or freeze dried compositions can be prepared using excipients such as polysaccharides {starch} and sodium chloride (¶ 115).

Claim 11 is rejected under 35 U.S.C. 103(a) as being unpatentable over Brocchini et al. (US 2002/0082362) in view of Neuenschwander et al. (US 5,665,831), as applied to claim 1 above, in further view of Shalaby (US 6,503,991).

Regarding claim 11: Brocchini et al. and Neuenschwander et al. render the basic claimed composition obvious [as set forth above with respect to claim 1], wherein Brocchini et al. disclose the diol may also comprise any diol suitable for use in biomaterials (¶ 91).

Brocchini et al. does not a specific diol comprising a carbonate. However, Shalaby teaches biocompatible block copolymers (abstract) comprising a pre-polymer prepared from an alkanediol containing a carbonate linkage (1:61-2:3). Brocchini et al. and Shalaby are analogous art because they are concerned with a similar technical difficulty, namely the preparation of biocompatible block copolymers prepared from diols. At the time of invention a person of ordinary skill in the art would have found it obvious to have combined a pre-polymer prepared from an alkanediol containing a carbonate linkage, as taught by Shalaby in the invention of Brocchini et al., and would have been motivated to do so since Shalaby suggests that carbonate linkages provide biomedical articles having controlled absorption and reduced hydrolytic instability (2:34-42).

Claims 15, 25, 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Brocchini et al. (US 2002/0082362) in view of Neuenschwander et al. (US 5,665,831), as applied to claims 1 and 14 above, in further view of Wise et al. (US 6,071,982).

Regarding claim 15, 25, 27: Brocchini et al. and Neuenschwander et al. render the basic claimed composition obvious [as set forth above with respect to claims 1 and 14], wherein the polymer-drug conjugate of the invention may also include buffers (¶ 112).

Brocchini et al. does not teach a specific buffer. However, Wise et al. teaches bioerodible polymers (abstract) comprising buffers such as calcium phosphate (5:21-59) and calcium phosphate fibers (6:58-59). Brocchini et al. and Wise et al. are analogous art because they are concerned with a similar technical difficulty, namely the preparation of biodegradable polymers comprising buffers. At the time of invention a person of ordinary skill in the art would have found it obvious to have combined calcium carbonate and/or calcium phosphate fibers as a buffer, as taught by Wise et al. in the invention of Brocchini et al., and would have been motivated to do so since Wise et al. suggests that calcium carbonate and calcium phosphate counteracts the effects of irritation, inflammation, and swelling caused by acidic products generated upon hydrolysis within the body (5:21-39).

Claims 20 and 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Brocchini et al. (US 2002/0082362) in view of Neuenschwander et al. (US 5,665,831), as applied to claim 19 above, in further view of Pathak et al. (US 6,923,986).

Regarding claims 20 and 22: Brocchini et al. and Neuenschwander et al. render the basic claimed composition obvious [as set forth above with respect to claim 19], wherein the composition can include additives such as antibiotics, antiseptics (¶ 112), bioactive agents {drugs}, and anticancer agents (¶99); as well as other additives (¶ 112).

Brocchini et al. does not teach growth factors or growth agents. However, Pathak et al. teaches biodegradable polymers for use in drug delivery and biomedical applications (1:16-18), wherein additives such as antibiotics, antivirals, drugs and growth factors can be used in the

composition; with specific growth factors including fibroblast growth factor {FGF} (11:8-36) and bone morphogenetic protein {BMP} (11:37-59). Brocchini et al. and Pathak et al. are analogous art because they are concerned with a similar technical difficulty, namely the preparation of biodegradable polymers comprising additives such as antibiotics. At the time of invention a person of ordinary skill in the art would have found it obvious to have combined FGF and BMP, as taught by Pathak et al. in the invention of Brocchini et al., and would have been motivated to do so since Pathak et al. suggests that additives such as FGF and BMP are suitable for use in biodegradable polymers for use in drug delivery and biomedical applications (11:8-36).

Claim 21 is rejected under 35 U.S.C. 103(a) as being unpatentable over Brocchini et al. (US 2002/0082362) in view of Neuenschwander et al. (US 5,665,831), as applied to claim 19 above, in further view of Törmäla et al. (US 6,579,533).

Regarding claim 21: Brocchini et al. and Neuenschwander et al. render the basic claimed composition obvious [as set forth above with respect to claim 19], wherein the composition can include additives such as antibiotics, antiseptics (¶ 112), bioactive agents {drugs}, and anticancer agents and bioactive proteins (¶99); as well as other additives (¶ 112).

Brocchini et al. does not teach a specific antibiotic. However, Törmäla et al. teaches bioabsorbable polymers containing antibiotics for use biomedical applications (1:5-26), wherein specific antibiotics include vancomycin (7:27-37). Brocchini et al. and Törmäla et al. are analogous art because they are concerned with a similar technical difficulty, namely the preparation of biodegradable polymers comprising additives such as antibiotics. At the time of invention a person of ordinary skill in the art would have found it obvious to have combined vancomycin, as taught by Törmäla et al. in the invention of Brocchini et al., and would have been motivated to do so since Törmäla et al. suggests that the antibiotic vancomycin is suitable for use in biodegradable polymers for use biomedical applications (7:27-37).

Claim 23 is rejected under 35 U.S.C. 103(a) as being unpatentable over Brocchini et al. (US 2002/0082362) in view of Neuenschwander et al. (US 5,665,831), as applied to claim 19 above, in further view of Uhrich (US 2002/0071822).

Regarding claim 23: Brocchini et al. and Neuenschwander et al. render the basic claimed composition obvious [as set forth above with respect to claim 19], wherein the polymer-drug conjugate contains doxorubicin (¶ 99, 104).

Brocchini et al. does not teach methotrexate. However, Uhrich teaches biocompatible/degradable polymers containing bioactive compounds (¶ 7), wherein specific bioactive compounds include doxorubicin and methotrexate (¶ 42). Brocchini et al. and Uhrich are analogous art because they are concerned with a similar technical difficulty, namely the preparation of biodegradable polymers comprising bioactive agents. At the time of invention a person of ordinary skill in the art would have found it obvious to have combined methotrexate, as taught by Uhrich in the invention of Brocchini et al., and would have been motivated to do so since Uhrich suggests that doxorubicin and methotrexate are equivalent bioactive agents (¶ 42) [see MPEP 2144.06].

Claim 24 is rejected under 35 U.S.C. 103(a) as being unpatentable over Brocchini et al. (US 2002/0082362) in view of Neuenschwander et al. (US 5,665,831), as applied to claim 19 above, in further view of Heller et al. (US 7,045,589).

Regarding claim 24: Brocchini et al. and Neuenschwander et al. render the basic claimed composition obvious [as set forth above with respect to claim 19], wherein the composition can include additives such as antibiotics, antiseptics (¶ 112), bioactive agents {drugs}, and anticancer agents and bioactive proteins (¶99); as well as other additives (¶ 112).

Brocchini et al. does not teach a pain killer. However, Heller et al. teaches biodegradable polymers (1:9-12; 5:3-16) containing active agents such as anti-inflammatory agents including ketorolac; and local anesthetics such as lidocaine and bupivacaine (8:22-67). Brocchini et al. and Heller et al. are analogous art because they are concerned with a similar technical difficulty, namely the preparation of biodegradable polymers comprising active agents. At the time of invention a person of ordinary skill in the art would have found it obvious to have combined anti-inflammatory agents including ketorolac; and local anesthetics such as lidocaine and bupivacaine, as taught by Heller et al. in the invention of Brocchini et al., and would have been motivated to do so since Heller et al. suggests that such active agents are suitable for use in biodegradable polymers for use biomedical applications (5:3-16; 8:22-67).

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MICHAEL PEPITONE whose telephone number is (571)270-3299. The examiner can normally be reached on M-F, 7:30-5:00 EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mark Eashoo can be reached on 571-272-1197. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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MFP
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/Mark Eashoo/
Supervisory Patent Examiner, Art Unit 1767